

1615 IFW



**TRANSMITTAL LETTER**  
**(General - Patent Pending)**

Docket No.  
**DC0266US.NP**

In Re Application Of: **Kitareewan et al.**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/564,070	January 10, 2006	Not yet assigned	26259	1615	5026

Title: **Compositions and Methods for Destabilizing Lysosomes to Increase Oncogenic or Aberrant Protein Degradation**

COMMISSIONER FOR PATENTS:

Transmitted herewith is:

**Courtesy Copy of International Preliminary Report on Patentability**

in the above identified application.

- ☒ No additional fee is required.
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- ☒ The Director is hereby authorized to charge and credit Deposit Account No. **50-1619** as described below.
- ☐ Charge the amount of \_\_\_\_\_
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- ☐ Payment by credit card. Form PTO-2038 is attached.

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*Jane Massey Licata*

Signature

Dated: **June 8**, 2006

Jane Massey Licata, Reg. No. 32,257

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on

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(Date)

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Signature of Person Mailing Correspondence

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Typed or Printed Name of Person Mailing Correspondence

cc:

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

FEB 28 2006

**PCT**

NOTIFICATION CONCERNING  
TRANSMITTAL OF COPY OF INTERNATIONAL  
PRELIMINARY REPORT ON PATENTABILITY  
(CHAPTER I OF THE PATENT COOPERATION  
TREATY)

(PCT Rule 44bis.1(c))

To:

LICATA, Jane, Massey  
Licata & Tyrrell P.C.  
66 E. Main Street  
Marlton, NJ 08053  
ETATS-UNIS D'AMERIQUE

Date of mailing ( <i>day/month/year</i> ) 16 February 2006 (16.02.2006)		
Applicant's or agent's file reference DC-0266		IMPORTANT NOTICE
International application No. PCT/US2004/024611	International filing date ( <i>day/month/year</i> ) 30 July 2004 (30.07.2004)	Priority date ( <i>day/month/year</i> ) 04 August 2003 (04.08.2003)
Applicant TRUSTEES OF DARTMOUTH COLLEGE et al		

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Athina Nickitas-Etienne

Facsimile No.+41 22 740 14 35

Facsimile No.+41 22 338 89 95

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference DC-0266	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2004/024611	International filing date ( <i>day/month/year</i> ) 30 July 2004 (30.07.2004)	Priority date ( <i>day/month/year</i> ) 04 August 2003 (04.08.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant TRUSTEES OF DARTMOUTH COLLEGE		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a).																								
2.	This REPORT consists of a total of 4 sheets, including this cover sheet.  In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 06 February 2006 (06.02.2006)
Facsimile No. +41 22 740 14 35	Authorized officer  <h3 style="text-align: center;">Athina Nickitas-Etienne</h3> Telephone No. +41 22 338 89 95

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
JANE MASSEY LICATA  
LICATA & TYRRELL P.C.  
66 E. MAIN STREET  
MARLTON, NJ 08053

REC'D 17 JAN 2005

WIPO PCT  
WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing (day/month/year) <b>13 JAN 2005</b>	
<b>FOR FURTHER ACTION</b> See paragraph 2 below	
Applicant's or agent's file reference <b>DC-0266</b>	
International application No. <b>PCT/US04/24611</b>	International filing date (day/month/year) <b>30 July 2004 (30.07.2004)</b>
Priority date (day/month/year) <b>04 August 2003 (04.08.2003)</b>	
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): A61F 13/00 and US Cl.: 424/400, 434, 422; 514/725, 82</b>	
Applicant <b>TRUSTEES OF DARTMOUTH COLLEGE</b>	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Lakshmi S Channavajjala <i>J. Roberts for</i> Telephone No. (571) 272-1600
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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/24611

**Box No. 1 Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/24611

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-7</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-7</u>	NO
Industrial applicability (IA)	Claims <u>1-7</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-7 lack novelty under PCT Article 33(2) as being anticipated by US 5,242,932 to Gandy et al (Gandy).

Gandy teaches a method of treating amyloidosis associated with Alzheimer's disease. Gandy teaches agents, which modulate or affect the intracellular trafficking and processing of proteins in the mammalian cell and suggest that these agents can be utilized to affect the trafficking and processing of amyloid precursor proteins (APP) and thus inhibiting the production of Alzheimer type and amyloidosis (col. 3 and col. 4). In particular, Gandy teaches chloroquine and its related derivatives such as primaquine. Gandy teaches that lysosomal acidification inhibitor, chloroquine, slows down the processing of APP to amyloid proteins (col. 6-8). Thus, the claimed method of identifying and the method of treating are inherent to the teachings of Gandy.

Claims 1-7 lack an inventive step under PCT Article 33(3) as being obvious over US 5,989,803 to Tabbas et al (Tabbas).

Tabbas teaches a method of treating a subject suffering from a condition associated with an extracellular zinc sphingomyelinase by administering an sphingomyelinase inhibitor. In the process of identifying the role of lysosome in the processing of sphingomyelinase-LDL (SM-LDL), Tabbas performed a set of experiments with 200micromolar chloroquine, an inhibitor is a known destabilizer of lysosome and the step of increasing the aberrant protein production is inherent to chlloquine. Tabbas also identifies that effect of chloroquine on the epidermal growth factor (EGF) observed that chloroquine blocked the degradation of EGF that occurs in lysosomes. Thus, Tabbas teaches chloroquine, a compound that destabilizes lysosomal protein degradat ion, which in turn increases the accumulation of proteins such as SM-LDL or epidermal growth factor and their association in disease processes, such as neuroegenarative diseases or multiple sclerosis. Thus, identifying the agents tht inhibit the lysosomal degradation of proteins and further, employing such enzymes in treating diseases or disorders associated with these inhibitors does not involve an inventive step.

Claims 1-7 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.